Ecofriendly Synthesis of some Heterocyclic compounds using Novel Methods

A proposed synopsis submitted to

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By

Mr. Pande Prasad Ramakant

Under the Supervision of

Dr. Niralwad Kirti S

Assistant Professor

Department of Chemistry

Nutan Mahavidyalaya Selu,

Dist. Parbhani

Research Centre

Shivaji College Parbhani

Dist Parbhani.

Swami Ramanand Teerth Marathwada University, Nanded, Maharashtra, India

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Introduction-

Heterocyclic compounds have attracted significant interest due to their useful biological and

pharmaceutical properties [1]. Many natural and synthetic drugs, dyes, pesticides are heterocyclic in nature [2]. Pyrazoles are synthesized by the reaction of 1,3-diketones with hydrazines and the reaction of α,β-unsaturated aldehydes and ketones with hydrazines [3,4]. For example, Fenpyroximate, a potent acaricide with a significant pyrazole ring in the structure, was found to display excellent acaricidal properties against some phytophagous mites. Among heterocyclic compound , biologically active nitrogen containing heterocycles contribute numerous applications in industry.

The Heterocyclic and its derivative contribute a broad range of synthetic and natural product and comprises a unique chemical, medicinal, pharmacological, biological, agrochemical properties.

in recent years several drugs have been synthesized from Heterocyclic and its derivative.

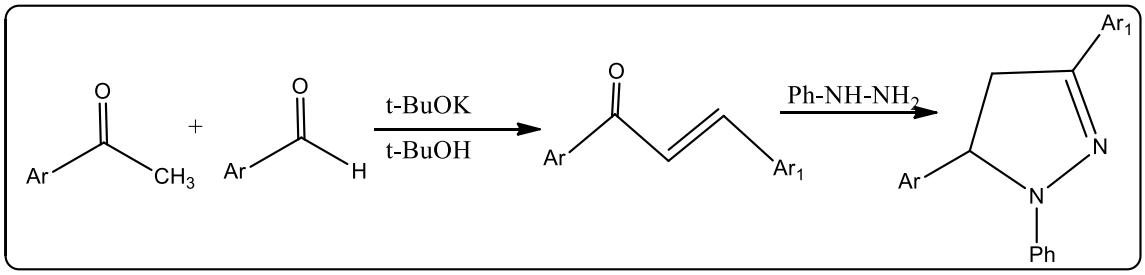
Heterocyclic derivative acts as an ligand and has an wide range of applications in co-ordination chemistry.Heterocyclic ring also expose its agrochemical properties and finds its application in pesticides, fungicides, herbicides, rodenticides etc including chlorfenapyr, fenpyroximate, fipronil, tebufenpyrad, tolfenpyrad and tralopyril.

Survey of literature-

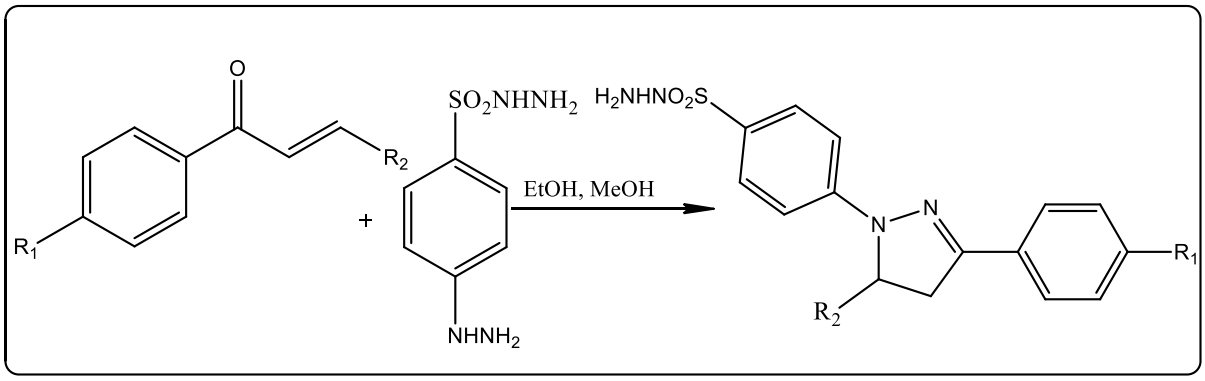
Efforts have been made constantly to introduce new methodologies and use of such a solvent which is environment friendly, increasing effective yield, reducing cost. One of the most promising challenges is to use traditionally used organic solvent which suffer from various health and environmental concern.

The use of microwave for the synthesis of solvent free reaction and reaction with solvent with less toxicity is proved to be environmental friendly, efficient in yield, cheaper. Furthermore, it can avoid the use of hazardous, expensive and toxic solvents can be environmental friendly.

B. Movassagh *et al* [5] developed a more suitable method to prepare the derivatives of 3,5-diaryl-1-phenyl-2-pyrazoline synthesized from phenylhydrazine with various chalcone derivatives via Claisen–Schmidt condensation. The reaction was conducted at room temperature in the existence of t-BuOK and anhydrous t-BuOH within short of time (3-13 min) with of 69-89 % yield.

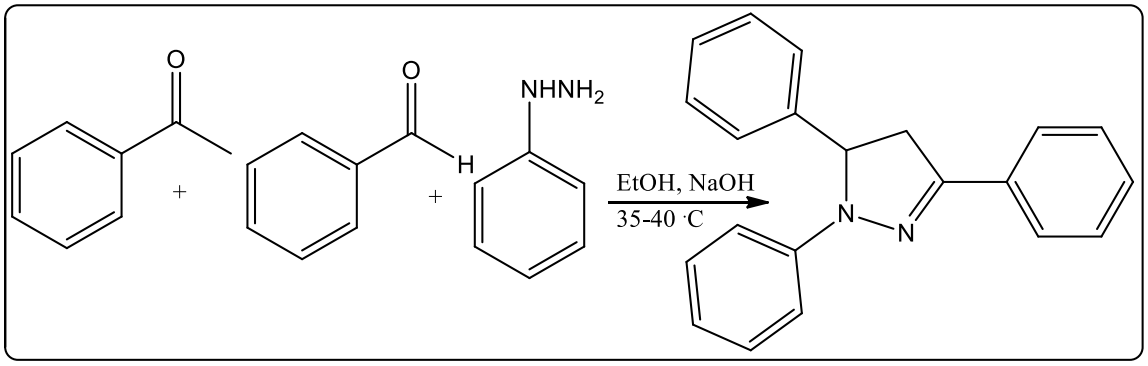


S. Hassan *et al* [6] reported some new pyrazoline and pyrazole derivatives have been prepared, and their physical properties were characterized. a series of benzosulfonamides pyrazolines via reaction of chalcone with modified phenyl hydrazine in presence of ethanol as a solvent to afford 87-90 % yield.

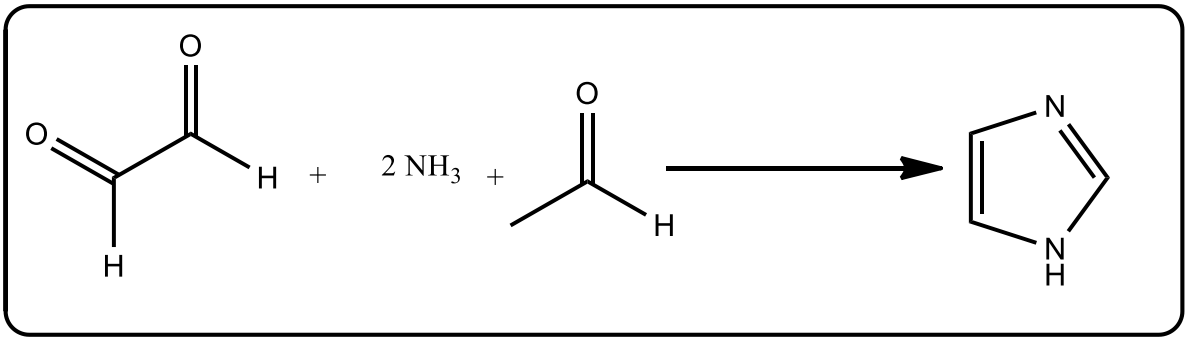


V.F. Traven *et al* [7] described one-pot method for the synthesis of 1,3,5-triaryl-2-pyrazolines. The synthesis comprised a reaction of aryl aldehydes, acetophenone and

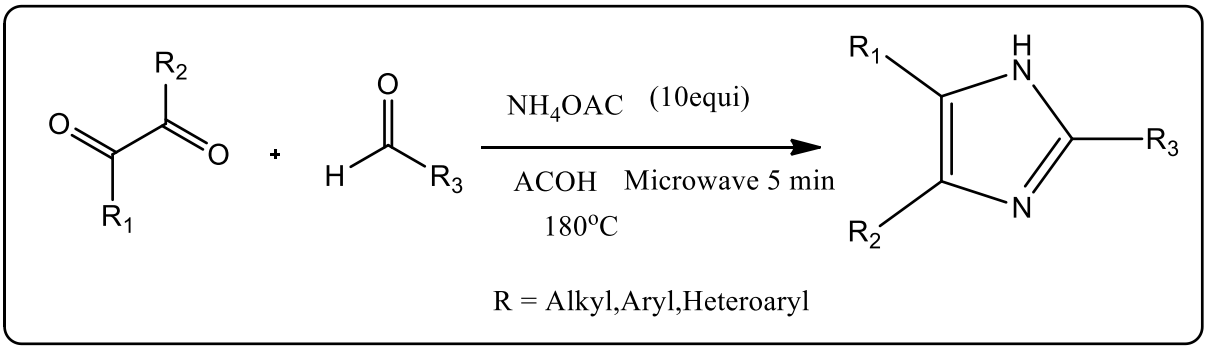
phenylhydrazine in the presence of NaOH as a base under reflux condition with more than 40 min. in ethanol to accomplish 78 % yield.



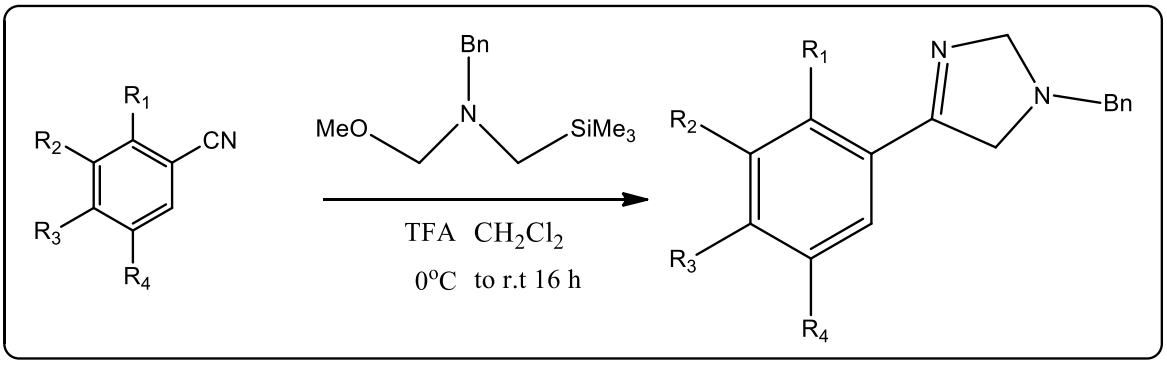
A. A. Gridnev *etal* [8] developed a mechanistic examination of the synthesis of imidazole and 1-alkylimidazoles has led to a superior synthesis starting from glyoxal, formaldehyde and alkylammonium chlorides.



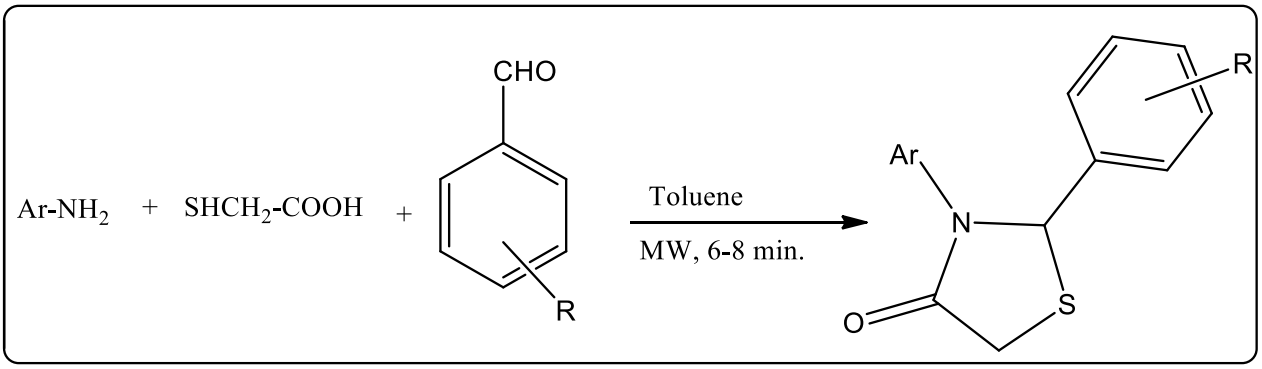
S. E. Wolkenberg *etal* [9] reported a simple, high-yielding synthesis of 2,4,5-trisubstituted imidazoles from 1,2- diketones and aldehydes in the presence of NH_4OAc is described. Under microwave irradiation, alkyl-, aryl-, and heteroaryl-substituted imidazoles are formed in yields ranging from 80 to 99%.



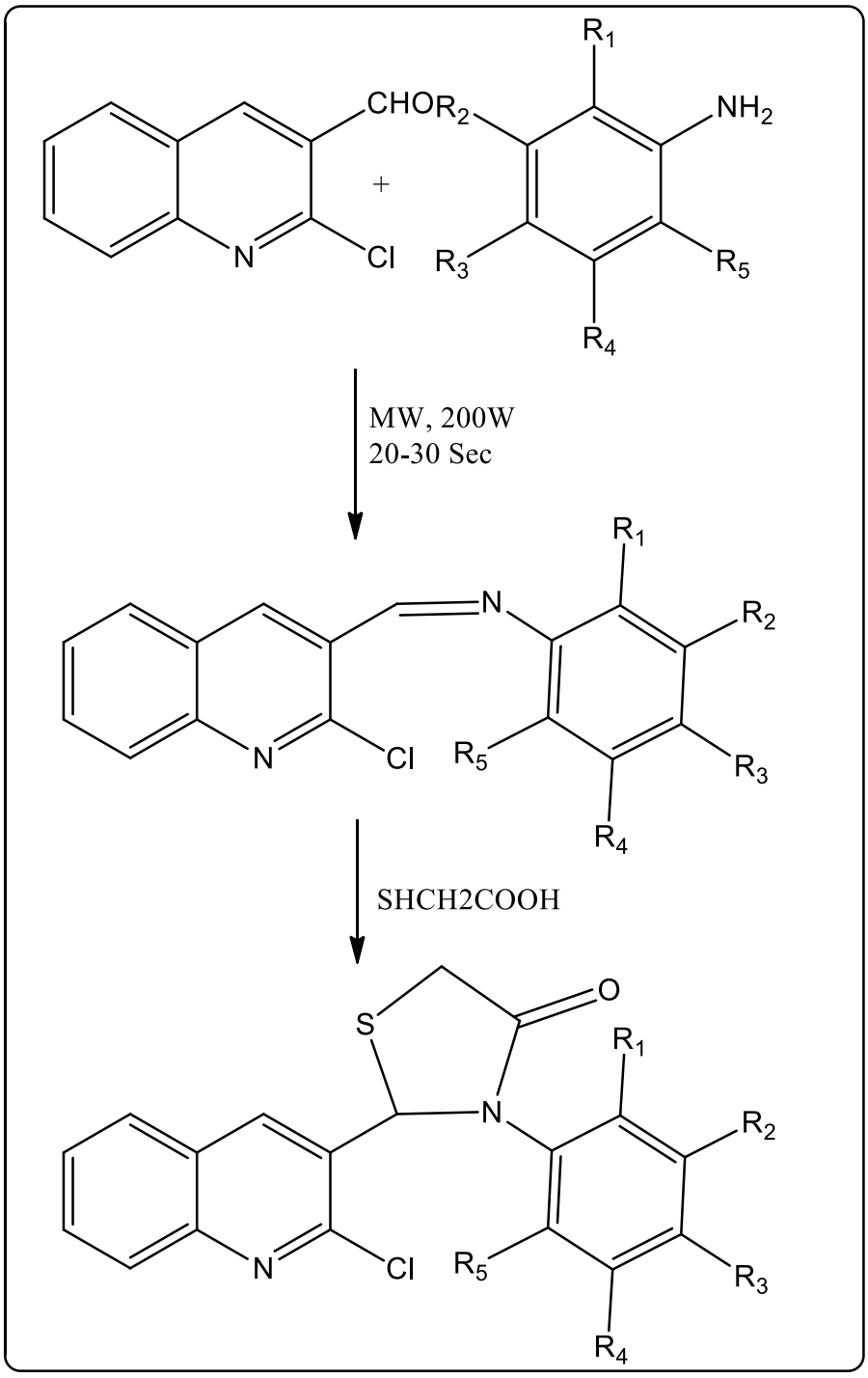
M. Beuvin *etal* [10] developed a efficient access to 4-aryl imidazole scaffolds is described in two steps and one operation. Cyanoarylimidazolines are easily obtained by a (3 + 2) heterocyloaddition involving cyanobenzenes as dipolarophiles and a non-stabilized azomethine ylide as an electron-rich 1,3-dipole. Oxidation of the crude mixture affords an efficient two-steps access to the corresponding imidazoles.



D. Sriram *et al.* [11] synthesized series of 1,3-thaizolidin-4-ones bearing variously unsubstituted diaryl ring at C-2 and N-3 positions and evaluated them for their anti-YFV activity. The synthesis of the 2,3-diaryl-1,3-thiazolidin-4-ones was done by reacting substituted benzaldehyde with equimolar amount of an appropriate substituted aromatic amine in the presence of an excess of mercaptoacetic acid in toluene utilizing microwave irradiation.



V. Tiwari *et al* [12] reported Zeolite 5A° for the synthesis of 2-(2-chloroquinoline-3-yl)-3-substituted phenyl thiazolidin-4-ones starting from N-aryl-2-chloroquinolin-3-yl-azomethine and thioglycolic acid under microwave irradiation.


R1
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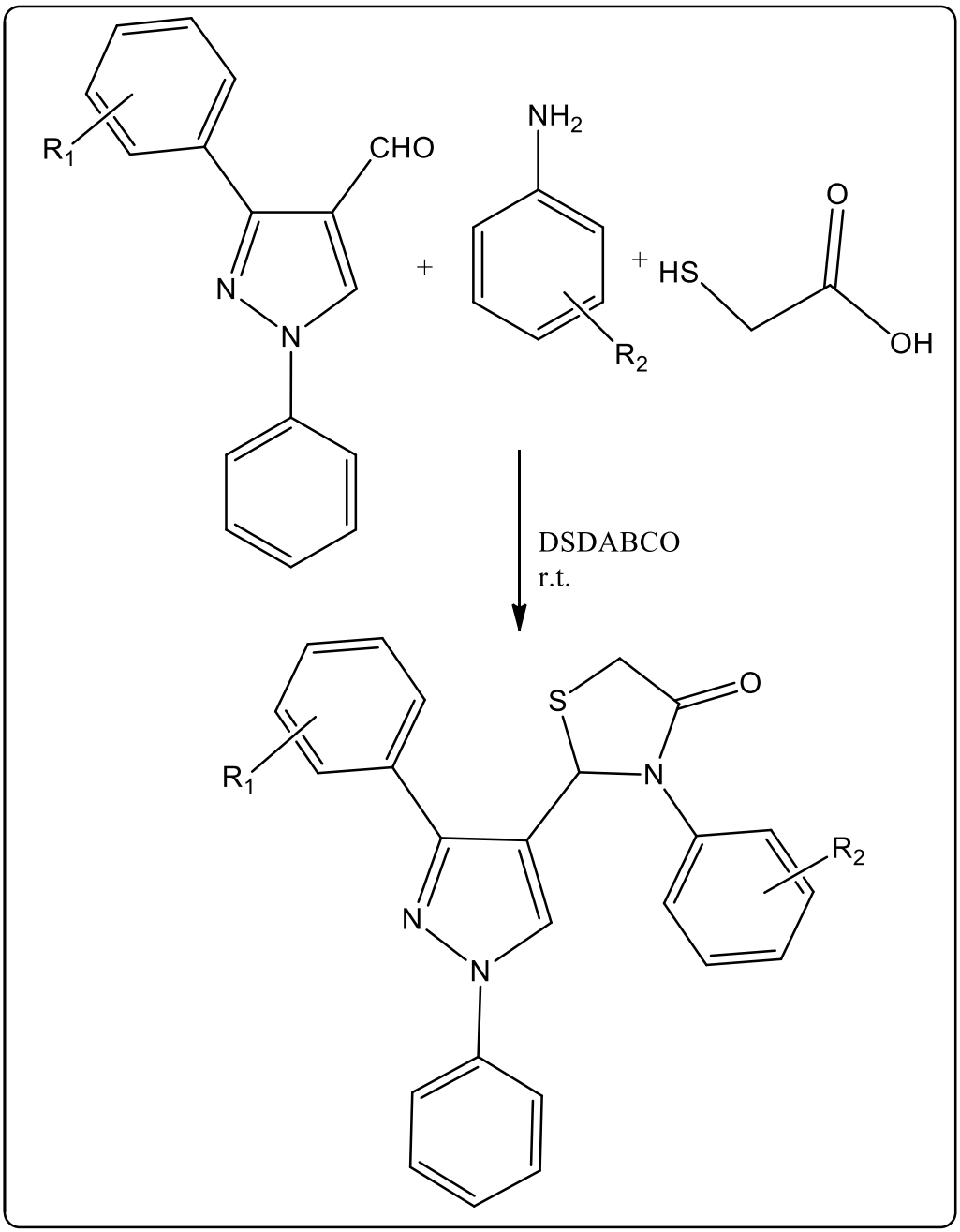
H. Taherkhorsand *et al* [13] developed an competent and simple procedure for the synthesis of novel pyrazolo-1,3-thiazolidine-4-ones using DSDABCOC as an ionic liquid. The simple workup together with the use of cheap, reusable and eco-friendly ionic liquid, is the notable trait of this novel procedure. this is the first report for the synthesis of 1,3-thiazolidine-4-ones containing a pyrazolyl moiety that increases the biological activity under solvent-free conditions.



National Significance-

The national significance of research on heterocyclic compounds is due to their potential applications in a number of fields, including:

Medicine: Heterocyclic compounds are used in the development of new drugs, such as antibiotics, anti-cancer agents, and anti-viral agents. For example, the antibiotic ciprofloxacin is a heterocyclic compound that is used to treat a variety of bacterial infections.

Agriculture: Heterocyclic compounds are used in the development of new pesticides and herbicides. For example, the herbicide glyphosate is a heterocyclic compound that is used to kill weeds.

Chemical industry: Heterocyclic compounds are used in the production of a variety of chemicals, such as plastics, dyes, and solvents. For example, the plastic nylon is made from a heterocyclic compound called hexamethylenediamine.

Food industry: Heterocyclic compounds are used in the production of flavors and food additives. For example, the artificial sweetener saccharin is a heterocyclic compound.

International Significance-

The international significance of research on heterocyclic compounds is immense. These compounds have been shown to have a wide range of biological activities, including antimicrobial, anticancer, and antiviral properties. They are also used in the synthesis of many important drugs, such as antibiotics, anticonvulsants, and antidepressants. In addition, heterocyclic compounds are used in a variety of industrial applications, such as the production of plastics, dyes, and pesticides.

Some of the specific international significance of research on heterocyclic compounds include:

The development of new drugs to treat diseases such as cancer, HIV/AIDS, and malaria.

The discovery of new ways to synthesize pharmaceutically important compounds.

- The development of new catalysts for industrial processes.
- The study of the structure and function of biological molecules.

- The investigation of the environmental impact of heterocyclic compounds.

  Research on heterocyclic compounds is a rapidly growing field, and it is expected to continue to produce important advances in the years to come.

  Here are some specific examples of the international significance of research on heterocyclic compounds:
- The antibiotic ciprofloxacin, which is used to treat a variety of bacterial infections, is a heterocyclic compound.
- The anticonvulsant drug phenytoin, which is used to treat epilepsy, is a heterocyclic compound.
- The antidepressant drug fluoxetine, which is sold under the brand name Prozac, is a heterocyclic compound.
- The pesticide DDT, which was once widely used but is now banned in many countries due to its environmental toxicity, is a heterocyclic compound.

Objectives of the Research-

Heterocyclic compound contain nitrogen by virtue of their specific activity could be applied for infectious diseases. literature survey reveals that the significant role in the development of pharmacological important molecule. synthesis of new Heterocyclic derivative gives an opportunity to explore new molecule and acts as an precursor in drugs synthesis, biological activity, stability, toxicity, specific properties of the individual mofits are encouraging and well documented.

Keeping in view these facts it was planned to synthesize nitrogen containing heterocycle that is Heterocyclic and its derivative, studying properties and biological activity of these compound.

The study of structure-activity relationship of the new compound will impart structural starting material for drug designing also the result of research may be useful in understanding mechanism of drugs action.

The main objectives of the present research work are as follows.

- Synthesis of some new Heterocyclic derivative.
- Development of new synthetic routes and purification methods for the newly proposed compounds.

- Characterization the new compounds by IR, ^{1}H NMR, ^{13}C NMR and also by elemental analysis.
- Studying biological activities of new compounds such as antimicrobial activity.
- Study of structure activity relationship with reference to biological activity.

Proposed Work Plan-

I Year-

Literature survey, final idea of the work, preliminary synthesis of compound.

II Year-

Synthesis of Heterocyclic compound by advanced methods, using microwave irradiation, water mediated reaction, dry media reaction and reaction using ecofriendly catalyst and solvent etc.

III Year-

Purification of the compound, analytical study of the compound (IR, NMR, MASS), publishing the work and thesis writing.

Methodology-

The steps involved condensation of different aldehyde and ketone in presence of base followed by cyclisation of either in stepwise manner or in a one pot has achieved successfully to obtain this class of heterocycle under different condition. Phosphorous oxychloride ($POCl_3$), dimethyl formamide, acetamide, hyrazine are the common reagent are used for the synthesis of Heterocyclic appended heterocyclic skeletons

These protocol provide convenient strategies of annelate different heterocyclic nuclei with widespread bioactive Heterocyclic thereby extending the categories of heterocyclic system. These strategies also provide valuable information for the future design of more active biological agents through various modification and derivatization

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